Comparative Evaluation of Thermoplastic Granulation Techniques on Tablet Properties of Meloxicam

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***Abstract*—Meloxicam, a widely used nonsteroidal anti-inflammatory drug, exhibits poor aqueous solubility and high crystallinity, which limit its dissolution rate and oral bioavailability when formulated as conventional tablets. The present study aimed to evaluate the effectiveness of thermoplastic granulation techniques in improving the tablet properties of meloxicam. Melt granulation, melt agglomeration, and hot-melt extrusion were employed as solvent-free processing methods using suitable thermoplastic binders and polymers. The prepared granules and tablets were evaluated for pre-compression parameters, post-compression characteristics, and in vitro dissolution behavior. Results demonstrated significant improvement in flowability, compressibility, mechanical strength, and dissolution performance for thermoplastic granulated formulations compared to conventional approaches. Among the evaluated techniques, hot-melt extrusion showed superior enhancement in dissolution and overall tablet quality. The study concludes that thermoplastic granulation techniques represent efficient and scalable strategies for improving the formulation performance of poorly soluble analgesic drugs such as meloxicam, with strong potential for industrial application.**

***Index Terms*—Meloxicam; Thermoplastic granulation; Melt granulation; Hot-melt extrusion; Dissolution enhancement; Tablet properties**

I. INTRODUCTION

Oral solid dosage forms, particularly tablets, remain the most widely used pharmaceutical delivery systems due to their convenience, patient compliance, cost-effectiveness, accurate dosing, and long-term stability. They account for a major proportion of marketed pharmaceutical products and are commonly preferred for chronic therapeutic conditions, including pain and inflammatory disorders. Despite their advantages, the formulation of poorly water-soluble drugs presents a significant challenge in oral drug delivery. Many nonsteroidal anti-inflammatory drugs (NSAIDs) exhibit low aqueous solubility and high crystallinity, resulting in slow dissolution rates and variable oral bioavailability. These limitations often lead to delayed onset of action and inconsistent therapeutic outcomes when conventional formulation techniques are employed. Conventional granulation methods, such as wet and dry granulation, are widely used to improve flowability and compressibility; however, they often involve the use of solvents, multiple processing steps, and extended processing times. These drawbacks have driven the development of solvent-free, advanced granulation approaches that are efficient, environmentally friendly, and suitable for modern pharmaceutical manufacturing. Thermoplastic granulation techniques, including melt granulation, melt agglomeration, and hot-melt extrusion, utilize thermoplastic binders that melt during processing and solidify upon cooling, leading to improved particle agglomeration and drug dispersion. These methods have shown considerable potential in enhancing the physicochemical and biopharmaceutical properties of poorly soluble drugs. Meloxicam, a preferential cyclooxygenase-2 (COX-2) inhibitor widely used in the treatment of osteoarthritis, rheumatoid arthritis, and other inflammatory pain conditions, exhibits poor aqueous solubility and high crystallinity. These characteristics make meloxicam an ideal candidate for evaluating the effectiveness of thermoplastic granulation techniques. The aim of the present study was to comparatively evaluate melt granulation, melt agglomeration, and hot-melt extrusion for improving the tablet properties of meloxicam. The objectives included assessment of pre-compression and post-compression parameters, in vitro dissolution behavior, drug release kinetics, and solid-state characterization

to identify the most effective thermoplastic granulation technique.

II. MATERIALS AND METHODS

2.1 Materials

Meloxicam was used as the active pharmaceutical ingredient (API) in the present study. Thermoplastic binders and polymers employed included polyethylene glycol 6000 (PEG 6000), poloxamer (188/407), glyceryl monostearate (GMS), and Soluplus®, selected based on their melting behavior and suitability for melt-based processing. Microcrystalline cellulose (MCC PH 102) was used as a diluent and dry binder. Disintegrants such as sodium starch glycolate and/or crospovidone were incorporated to facilitate tablet disintegration. Magnesium stearate was used as a lubricant. All materials were of pharmaceutical grade and used as received.

2.2 Preparation of Granules

2.2.1 Melt Granulation

Melt granulation was carried out using a high-shear mixer. The thermoplastic binder was heated above its melting point and added to the powder blend containing meloxicam and excipients under continuous mixing. Granulation was continued until uniform agglomerates were formed, followed by cooling and sieving to obtain granules of suitable size.

2.2.2 Melt Agglomeration

In melt agglomeration, the binder was melted and sprayed or added onto the moving powder bed containing meloxicam under controlled mixing conditions. The molten binder facilitated particle agglomeration, forming spherical or irregular agglomerates. The agglomerates were cooled, dried if necessary, and sieved prior to further processing.

2.2.3 Hot-Melt Extrusion (HME)

Hot-melt extrusion was performed using a twin-screw extruder. Meloxicam was blended with selected polymers and fed into the extruder. The process was carried out at controlled temperature zones, screw speed, and feed rate to ensure uniform mixing and drug dispersion. The extrudates were cooled, milled, and sieved to obtain granules suitable for tableting.

2.2.4 Process Parameters and Formulation Composition

Critical process parameters such as processing temperature, mixing speed, residence time, and binder concentration were optimized for each technique to ensure uniform granule formation without thermal degradation of meloxicam.

2.3 Pre-Compression Studies

Prepared granules were evaluated for pre-compression properties, including bulk density and tapped density using standard methods. Flow behavior was assessed by measuring the angle of repose. Compressibility and flow characteristics were further evaluated by calculating Carr's index and Hausner ratio. Particle size distribution was determined by sieve analysis to assess granule size uniformity.

2.4 Tablet Compression

Granules obtained from each granulation technique were blended with required quantities of disintegrant and lubricant and compressed into tablets using a rotary tablet compression machine. Compression force and tablet weight were kept constant across all formulations to enable meaningful comparison.

2.5 Post-Compression Evaluation

Compressed tablets were evaluated for weight variation, hardness, friability, and disintegration time according to pharmacopeial guidelines. Drug content uniformity was determined by assaying tablets for meloxicam content using a suitable validated analytical method.

2.6 In Vitro Dissolution Studies

Dissolution studies were performed using USP Apparatus II (paddle method). The dissolution medium, temperature, paddle speed, and sampling intervals were selected based on pharmacopeial recommendations for meloxicam. Samples were withdrawn at predetermined time intervals and analyzed for drug content. Comparative dissolution profiles were constructed, and dissolution efficiency (%DE) was calculated.

2.7 Drug Release Kinetics

Dissolution data were fitted into various kinetic models, including zero-order, first-order, Higuchi, and Korsmeyer–Peppas models, to elucidate the drug

release mechanism and evaluate the influence of thermoplastic granulation techniques on release behavior.

2.8 Analytical Characterization

Fourier Transform Infrared (FTIR) spectroscopy was used to assess possible drug–excipient interactions. Differential Scanning Calorimetry (DSC) was performed to evaluate thermal behavior and solid-state transitions. X-ray Powder Diffraction (XRPD) analysis was conducted to study crystallinity changes, while Scanning Electron Microscopy (SEM) was used to examine surface morphology and granule structure.

2.9 Statistical Analysis

All experimental results were expressed as mean ± standard deviation (SD). Statistical analysis was performed using one-way analysis of variance (ANOVA) to determine significant differences among formulations prepared by different granulation techniques. A p-value less than 0.05 was considered statistically significant.

III. RESULTS AND DISCUSSION

3.1 Pre-Compression Properties

Granules prepared using thermoplastic granulation techniques exhibited significant improvement in pre-compression properties compared to conventional blends. Bulk and tapped density values indicated better packing ability, while reduced Carr's index and Hausner ratio reflected improved compressibility. Angle of repose measurements confirmed enhanced flowability, particularly for granules prepared by hot-melt extrusion, followed by melt granulation and melt agglomeration. Improved particle size distribution and reduced fines contributed to uniform die filling during tablet compression.

3.2 Post-Compression Properties

Tablets prepared from thermoplastic granulated meloxicam showed uniform weight, acceptable hardness, and friability values within pharmacopeial limits. Melt-based binders contributed to stronger interparticle bonding, resulting in tablets with improved mechanical strength. Disintegration time was optimized by the presence of suitable super disintegrants, ensuring rapid tablet breakup despite increased hardness. Drug content uniformity across all formulations remained within acceptable limits, indicating effective drug distribution.

3.3 Dissolution Behavior and Drug Release Kinetics

Thermoplastic granulation techniques significantly enhanced the dissolution rate of meloxicam compared to conventional formulations. Among the evaluated methods, hot-melt extrusion demonstrated the highest dissolution efficiency, followed by melt granulation and melt agglomeration. The improved dissolution was attributed to reduced crystallinity, enhanced wettability, and formation of solid dispersions. Drug release kinetics indicated diffusion-controlled release behavior, with dissolution data fitting best to the Higuchi and Korsmeyer–Peppas models.

3.4 Solid-State Characterization

FTIR analysis confirmed the absence of chemical interactions between meloxicam and excipients, indicating formulation compatibility. DSC thermograms showed reduced or shifted melting endotherms, suggesting partial or complete amorphization of meloxicam in thermoplastic formulations. XRPD patterns revealed decreased peak intensity, further supporting reduced crystallinity. SEM images demonstrated uniform granule morphology and improved surface characteristics in melt-processed formulations.

3.5 Statistical Outcomes

Statistical analysis using one-way ANOVA revealed significant differences ($p < 0.05$) among granulation techniques for key parameters such as flow properties, hardness, disintegration time, and dissolution rate. Hot-melt extrusion showed statistically superior performance compared to melt granulation and melt agglomeration, confirming its effectiveness as an advanced thermoplastic granulation technique for improving tablet properties of meloxicam.

IV. CONCLUSION

The present study demonstrated that thermoplastic granulation techniques significantly improve the tablet properties of meloxicam, a poorly soluble analgesic drug. All melt-based approaches enhanced pre-compression characteristics, tablet mechanical strength, and dissolution behavior compared to conventional processing methods. Among the

evaluated techniques, hot-melt extrusion (HME) exhibited the most pronounced improvement in flowability, compressibility, solid-state modification, and dissolution efficiency, indicating superior drug dispersion within the polymeric matrix. The findings confirm that thermoplastic granulation is a robust and solvent-free formulation strategy capable of overcoming solubility-related challenges associated with meloxicam. Moreover, the outcomes of this study highlight the broader relevance of these techniques for improving the oral delivery of other poorly water-soluble analgesic drugs, offering strong potential for industrial application and scalable pharmaceutical manufacturing.

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